

CLAIMS

1. A method for identifying a platelet clearance antagonist, comprising:
Contacting a chilled platelet with a liver macrophage in the presence and in the
absence of a test molecule; and
- 5 Detecting binding of the chilled platelet to the liver macrophage,
Wherein a reduction in the binding in the presence of the test molecule relative to
the binding in the absence of the test molecule indicates that the test molecule is a
platelet clearance antagonist.
2. A method for identifying a platelet clearance antagonist, comprising:
- 10 Contacting an isolated platelet ligand with a liver macrophage in the presence
and in the absence of a test molecule; and
detecting binding of the platelet ligand to the liver macrophage, wherein a
reduction in the binding in the presence of the test molecule relative to the binding in the
absence of the test molecule indicates that the test molecule is a platelet clearance
- 15 antagonist.
3. A method for identifying a platelet clearance antagonist, comprising:
contacting an isolated platelet ligand with an isolated liver macrophage receptor
in the presence and in the absence of a test molecule; and
detecting binding of the platelet ligand to the liver macrophage receptor, wherein
- 20 a reduction in the binding in the presence of the test molecule relative to the binding in
the absence of the test molecule indicates that the test molecule is a platelet clearance
antagonist.
4. A method for identifying a platelet clearance antagonist, comprising:
Contacting a chilled platelet with an isolated liver macrophage receptor in the
- 25 presence and in the absence of a test molecule; and
detecting binding of the chilled platelet to the liver macrophage receptor, wherein
a reduction in the binding in the presence of the test molecule relative to the binding in
the absence of the test molecule indicates that the test molecule is a platelet clearance
antagonist.
- 30 5. The method of any of claims 1-4, inclusive, wherein the platelet clearance
antagonist is a platelet antagonist.
6. The method of claim 5, wherein the platelet antagonist binds to a platelet ligand
selected from the group of platelet ligands provided in Table 1.

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7. The method of claim 5, wherein the platelet antagonist binds to a platelet ligand that is vWfR or a subunit thereof.

8. The method of any of claims 1-4, inclusive, wherein the platelet clearance antagonist is a liver macrophage receptor antagonist.

5 9. The method of claim 8, wherein the liver macrophage receptor is a Kupffer cell receptor antagonist.

10. The method of claim 8, wherein the liver macrophage receptor antagonist binds to a liver macrophage receptor selected from the group of liver macrophage receptors provided in Table 1.

10 11. The method of claim 8, wherein the liver macrophage receptor antagonist binds to a liver macrophage receptor that is $\alpha M\beta 2$.

12. The method of claim 1, wherein detecting binding of the platelet to the liver macrophage comprises detecting phagocytosis of the platelet by the macrophage.

13. A method for preparing a platelet antagonist-treated platelet for transfusion,
15 comprising:

Contacting a chilled platelet with a platelet antagonist under conditions to permit the chilled platelet antagonist to bind to a platelet ligand on the chilled platelet and, thereby, form a platelet antagonist-treated platelet.

14. The method of claim 13, wherein the platelet antagonist selectively binds to a
20 platelet ligand identified in Table 1.

15. The method of claim 13, wherein the platelet antagonist selectively binds to vWfR or a subunit thereof.

16. The method of claim 13, 14, or 15, wherein the platelet antagonist is an antibody or antibody fragment.

25 17. The method of claim 13, wherein contacting is performed after the platelets are chilled.

18. The method of claim 13, wherein contacting is performed in a platelet bag.

19. The method of claim 13, wherein the chilled platelets are treated with at least one of a first agent for inhibiting actin filament severing and a second agent for inhibiting
30 actin polymerization.

20. The method of claim 19, wherein the chilled platelets are treated with a first agent for inhibiting actin filament severing.

21. The method of claim 19, wherein the first agent is an intracellular calcium chelator.

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22. The method of claim 21, wherein the intracellular calcium chelator is selected from the group consisting of: QUIN, STIL, FURA, MATA, INDO, and derivatives thereof.
23. The method of claim 19, wherein the chilled platelets are treated with a second agent for inhibiting actin polymerization.
24. The method of claim 19, wherein the second agent is a cytochalasin.
25. The method of claim 24, wherein the cytochalasin is selected from the group consisting of: cytochalasin B and dihydro-cytochalasin B.
26. The method of claim 19, wherein the chilled platelets are treated with a first agent for inhibiting actin filament severing and a second agent for inhibiting actin polymerization.
27. The method of claim 26, wherein the first agent is an intracellular calcium chelator and the second agent is a cytochalasin.
28. The method of claim 27, wherein the intracellular calcium chelator is selected from the group consisting of QUIN, STIL, FURA, MATA, INDO, and derivatives thereof.
29. The method of claim 27, wherein the cytochalasin is selected from the group consisting of cytochalasin B and dihydro-cytochalasin B.
30. The method of claim 13, further comprising the step of separating the platelet antagonist-treated platelet from the platelet antagonist that has not bound to a chilled platelet.
31. The method of claim 13 or 30, further comprising the step of contacting the chilled platelet or the platelet antagonist-treated platelet with a liver macrophage receptor antagonist.
32. The method of claim 19, wherein the liver macrophage receptor antagonist binds to a liver macrophage receptor selected from the group of liver macrophage receptors provided in Table 1.
33. The method of claim 32, wherein the liver macrophage receptor antagonist binds to a liver macrophage receptor that is $\alpha M\beta 2$.
34. The method of claims 13, 30, or 31, further comprising the step of administering the platelet antagonist-treated platelet to a subject.
35. A method for forming a medicament, comprising:
placing a plurality of chilled platelets and one or more platelet clearance antagonists in a pharmaceutically acceptable carrier.

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36. The method of claim 35, wherein the platelet clearance antagonist is a platelet antagonist.

37. The method of claim 35, wherein the platelet clearance antagonist is a liver macrophage receptor antagonist.

5 38. A composition comprising:
A plurality of platelets; and
One or more platelet clearance antagonists.

39. The composition of claim 38, wherein the composition comprises a first platelet clearance antagonist that is a platelet antagonist and a second platelet clearance
10 antagonist that is a liver macrophage

40. The composition of claim 38, wherein the platelet clearance antagonist is a platelet antagonist.

41. The composition of claim 40, wherein the platelet clearance antagonist is a liver macrophage receptor antagonist.

15 42. The composition of claim 38, wherein the composition is contained in a platelet bag.

43. The composition of claim 38, wherein the platelet clearance antagonist is a platelet antagonist that selectively binds to a platelet ligand identified in Table 1.

44. The composition of claim 43, wherein the platelet antagonist selectively binds to
20 vWfR or a subunit thereof.

45. The composition of claim 38, wherein the platelet clearance antagonist is a liver macrophage receptor antagonist that selectively binds to a liver macrophage receptor identified in Table 1.

46. The composition of claim 45, wherein the liver macrophage receptor antagonist
25 selectively binds to α M β 2.

47. The composition of claim 38, further comprising a pharmaceutically acceptable carrier.

48. A method for increasing platelet circulatory time, comprising:
Administering to a subject in need of such treatment, a composition comprising:
30 One or more platelet clearance antagonists in an amount effective to increase platelet circulatory time in the subject.

49. The method of claim 48, wherein the composition comprises a first platelet clearance antagonist that is a platelet antagonist and a second platelet clearance antagonist that is a liver macrophage

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50. The method of claim 48, wherein the platelet clearance antagonist is a platelet antagonist.

51. The method of claim 50, wherein the platelet clearance antagonist is a liver macrophage receptor antagonist.

5 52. The method of claim 48, wherein the composition is contained in a platelet bag.

53. The method of claim 48, wherein the platelet clearance antagonist is a platelet antagonist that selectively binds to a platelet ligand identified in Table 1.

54. The method of claim 53, wherein the platelet antagonist selectively binds to vWfR or a subunit thereof.

10 55. The method of claim 48, wherein the platelet clearance antagonist is a liver macrophage receptor antagonist that selectively binds to a liver macrophage receptor identified in Table 1.

56. The method of claim 55, wherein the liver macrophage receptor antagonist selectively binds to $\alpha M\beta 2$.

15 57. A method of treating a subject in need of platelets, comprising:

Administering to the subject,

(1) a first composition comprising:

A plurality of chilled platelets; and

One or more platelet clearance antagonists; or

20 (2) a second composition comprising:

a plurality of platelet-antagonist-treated platelets,

Wherein the first composition or the second composition is administered in an amount effective to treat the subject.

25 58. The method of claim 57, wherein the administering the second composition further includes administering a liver macrophage receptor antagonist to the subject.

59. The composition of claim 57, wherein the composition comprises a first platelet clearance antagonist that is a platelet antagonist and a second platelet clearance antagonist that is a liver macrophage receptor antagonist.

30 60. The composition of claim 57, wherein the platelet clearance antagonist is a platelet antagonist.

61. The composition of claim 60, wherein the platelet clearance antagonist is a liver macrophage receptor antagonist.

62. The composition of claim 57, wherein the composition is contained in a platelet bag.

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63. The composition of claim 57, wherein the platelet clearance antagonist is a platelet antagonist that selectively binds to a platelet ligand identified in Table 1.

64. The composition of claim 63, wherein the platelet antagonist selectively binds to vWfR or a subunit thereof.

5 65. The composition of claim 57, wherein the platelet clearance antagonist is a liver macrophage receptor antagonist that selectively binds to a liver macrophage receptor identified in Table 1.

66. The composition of claim 65, wherein the liver macrophage receptor antagonist selectively binds to $\alpha\text{M}\beta 2$.

10 67. A method for identifying a platelet lesion cleavage agent, comprising:

Contacting a chilled platelet with a liver macrophage in the presence and in the absence of a test cleavage agent; and

Detecting binding of the chilled platelet to the liver macrophage,

15 Wherein an increase in the binding in the presence of the test cleavage agent relative to the binding in the absence of the test cleavage agent indicates that the test molecule is a platelet lesion cleavage agent.

68. The method of claim 67, wherein test cleavage agent is selected from the group consisting of enzymes that cleave carbohydrates.

20 69. The method of claim 68, wherein the enzyme is a galactosidase, a glucosidase, a mannosidase.

70. The method of claim 67, wherein detecting binding of the chilled platelet to the liver macrophage comprises detecting phagocytosis of the chilled platelet by the liver macrophage.

25 71. The method of claim 67, wherein the platelet lesion comprises surface expression of vWfR or a subunit thereof by the chilled platelet.

72. The method of claim 67, further comprising the step of contacting the platelet lesion cleavage agent with a chilled platelet under conditions to permit the platelet lesion cleavage agent to cleave a platelet lesion on a chilled platelet.

73. A platelet prepared in accordance with the method of claim 72.

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